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AWARD NUMBER DAMD17-94-J-4318

TITLE: Evaluation of a Digital Telemammography System: A Model
for a Regional System

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REPORT DATE: April 1998

TYPE OF REPORT: Annual

PREPARED FOR: Commander
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release;
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19980721 160

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

1. AGENCY USE ONLY (Leave blank)

2. REPORT DATE
April 1998

3. REPORT TYPE AND DATES COVERED
Annual (15 Sep 96 - 14 Oct 97)

4. TITLE AND SUBTITLE
Evaluation of a Digital Telemammography System: A Model for a Regional System

5. FUNDING NUMBERS
DAMD17-94-J-4318

6. AUTHOR(S)
de Paredes, Ellen Shaw, M.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
University of Virginia
Charlottesville, Virginia 22906

8. PERFORMING ORGANIZATION
REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING
AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT (Maximum 200 words)

14. SUBJECT TERMS
Breast Cancer

15. NUMBER OF PAGES
49

16. PRICE CODE

17. SECURITY CLASSIFICATION
OF REPORT
Unclassified

18. SECURITY CLASSIFICATION OF THIS
PAGE
Unclassified

19. SECURITY CLASSIFICATION
OF ABSTRACT
Unclassified

20. LIMITATION OF ABSTRACT
Unlimited

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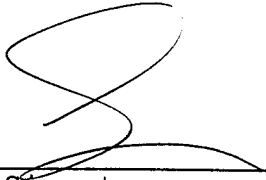
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Date

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April 1998

TELEMAMMOGRAPHY SYSTEM: A MODEL FOR A REGIONAL SYSTEM

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PURPOSE:

The research hypothesis being tested is that a telemammography system provides a mechanism for digitizing, transmitting, archiving, and displaying mammograms so that a trained radiologist utilizing grayscale monitors (2k x 2k x 8/12 bits) can interpret the images with an accuracy level sufficient for primary diagnosis. A new metric for measuring the performance of telemammography systems has been developed, throughput/cost ratio. This metric provides a measure for comparing analog to digital mammography systems. This metric has been employed in comparing manufacturing processes, i.e. jobs/sec/cost (1). A ROC curve analysis (2) is utilized to compare the accuracy of interpretation of analog images versus digitized images.

The hypothesis is being tested by utilizing a laser film digitizer with a 50-micron pixel size and by performing ROC studies to compare conventional analog screen-film mammography with digitized screen-film mammograms displayed on grayscale workstations (two monitors, each 2k x 2k x 8/12 bits). The wide area network (WAN) being utilized are terrestrial and satellites links. The goal of this study is to determine the requirements to deliver high quality, high resolution mammography images from remote locations that may not have a terrestrial data communications infrastructure available.

DESCRIPTION OF EXPERIMENTAL PROCEDURES:

A series of retrospectively collected 200 normal mammograms and 200 abnormal mammograms containing a single lesion including masses, calcifications, dilated lactiferous ducts, and asymmetric densities were collected for conducting a ROC analysis. The mammographic and pathologic findings were classified using the terminology of the American College of Radiology Lexicon. The ROC study, which used 12 readers compares analog screen-film mammograms and the mammograms which were digitized at 50 microns spot size. The

digitized analog screen-film mammograms were archived into a database. A comparison ROC curve analysis of the digitized mammograms is being conducted by displaying them on a 2k x 2k x 8/12 bit grayscale workstation using two monitors. An evaluation performance is being conducted using the metrics of throughput and throughput-to-cost-ratio. The throughput and throughput/cost ratio is based on the method of Jackson Network Analysis (3) and has been completed on the analog system. The calculations are based on a resource allocation table in which the average time required for each step is measured as applicable for each resource. A satellite transmission of mammograms is underway between the University of Virginia, the Cleveland Clinic Foundation, and the NASA Lewis Research Center (ACTS Project).

A softcopy display protocol has been developed and is being implemented to review the images in a similar format to the manner in which they are interpreted on a viewbox

SUMMARY OF RESULTS TO DATE:

An ROC analysis has been conducted on the 400 analog screen film mammograms. For all readers the results of the ROC analog images varied 10% from the 0.83 area under the ROC curve, which is a desirable result, reflecting proper case selection. A ROC analysis is underway for the two monitor, grayscale 2k x 2k workstation display of the digitized mammograms. The results of the throughput analysis of the analog images showed that the technologist was the bottleneck (0.041 jobs/minute) and the throughput to cost ratio was 0.001203. Our measure of luminance of the workstation shows the average luminance level to be 1/10 that of the mammography viewbox. The contrast range for the grayscale display is 20% lower than that of analog images.

CONCLUSIONS:

The resulting softcopy display protocol for the digitized screen film mammograms reduces the throughput by a factor of one-half. The digitized screen film images (4k x 4k x 12 bits) presents a difficult display protocol for a 2k x 2k x 8/12 bits monitor. Additional challenges to display are the presentation of 4 images on 2 monitors as well as the review of prior images for comparison. Because of the lower contrast range of the grayscale displays, image processing (window and level functions) is needed on the softcopy.

METHODS:

Image Selection.

A database of 200 normal screen-film mammography examinations and 200 abnormal screen-film mammography examinations have been collected. Each examination contains the following: image study performed; results; description of mammographic findings if abnormal (the same as the BIRADS); type and report of biopsy performed; demographics; procedural and diagnostic radiation exposure; and clinical follow-up. The abnormal films comprise a representative sample of pathological diagnosed breast lesions in

the population served by the University of Virginia and MCV. The normal films have been substantiated by clinical follow-up and are age matched to the overall parenchymal density of the abnormal films. All patient data and names were blocked and a case number assigned.

DIGITIZED IMAGE DATABASE

The collected database of analog mammographic films was converted into digital arrays using a laser film digitizer with a 50 micron pixel spot size and 12 bits per pixel (Lumisys, Sunnyvale, CA, Model 150 with a 50-micron spot size). The laser film digitizer was connected to a sun workstation 9SPARC Model 40) and connected to an internet connectivity. All patient data were removed and a case number assigned to each digitized case. This image database is being recorded on a CD-ROM for use by other researchers. The digitized images are archived into a database and archived on both a hard drive disk and a Tape drive.

The laser film digitizer uses an analog film SMPTE pattern once a week to provide an adequate quality control. Additionally, the laser film digitizer is calibrated once a week using the protocol provided by the manufacturer. Each digitized image was displayed on a grayscale display workstation to assure proper digitization of the screen-film images.

IMAGE GRADING AND READING.

The readers use a 5-point graded response. Each reader completed a worksheet form for each image, requiring a response to the following six questions by circling the selected graded response. The pathology reports of the biopsies served as ground truth.

Masses:

1. (definitely not present); 2. (probably not present);
3. (equivocal); 4. (probably present); 5. (definitely present)

Microcalcifications:

1. (definitely not present); 2. (probably not present);
3. (equivocal); 4. (probably present); 5. (definitely present).

Dilated lactiferous ducts:

1. (definitely not present); 2. (probably not present);
3. (equivocal); 4. (probably present); 5. (definitely present).

Focal areas of asymmetry or architectural distortion:

1. (definitely not present); 2. (probably not present);
3. (equivocal); 4. (probably present); 5. (definitely present).

Thickening or retraction of the skin;

1. (definitely not present); 2. (probably not present);
3. (equivocal); 4. (probably present); 5. (definitely present).

Diagnosis of image:

1. (definitely benign); 2. (probably benign);
3. (equivocal); 4. (probably malignant); 5. (definitely malignant)

Images were presented to the set of readers first as analog mammographic films. The films were hung in sets on several rollerscopes in the department. The readers read each image and responded to the above six questions. The readers are just now starting to read the digitized film images on a grayscale workstation. It is believed that enough time has passed from the analog screen film readings that the readers will not remember the cases. The readers may utilize a magnifying glass as an option if they wish. A random number generator is being used to modify the order of presentation on the grayscale display as compared to the presentation of the analog mammography images. Reader data is recorded in a notebook, one page per mammographic exam. The reader data is then entered into a database and a ROC analysis performed for each of the six questions responded to by the readers.

STATISTICAL CONSIDERATIONS

In selecting the sample size, we have used two methods to increase the reliability of the calculation. In the first method, we have chosen type I error to be equal to 0.05 (1.96) for a two tailed test and type II error to be equal to 0.20 (0.84). Hence the power index (PI) is 2.8. The sample size is given by n equal to $((PI \times SE / (A1 - A2))^2$ squared where $A1$ is the area under the ROC curves for analog films and $A2$ is the area under the ROC curves for digitized and grayscale displayed images. We estimate the standard error to be 0.5 for 12 readers, all providing primary coverage in mammography. We assume the differences in the means of the areas under the two ROC curves to be 10%. Then the number of samples per population is 196 or approximately 200 pairs of images. Hence we will require 200 normal and 200 abnormal mammograms.

In a second method that confirms the findings of the first approach, we assume the following; alpha error 0.05, beta error 0.2, power 80%, and the expected difference between the areas underneath the ROC curves for the digital ($A2$), and analog ($A1$) mammographic films as 0.1. This expected difference is the minimum difference that we consider clinically important. Specifically, we are estimating $A1$ to be 0.85 and $A2$ to be 0.75. Since each reader will review the same sample of cases, we will use a correlation coefficient conservatively estimated at 0.3. Using the methods of Hanley and McNeil and a two-sided test of significance, we calculate that with a single reader we will require 120 cases each of abnormal and normal films. Thus, if the difference between $A1$ and $A2$ is as estimated above, we will have a greater than 80% chance with a single reader of detecting a statistically significant difference in diagnostic performance with 120 pairs of normal and abnormal cases. Using additional readers (12 total) and cases (200 each of normal and abnormal) will give us a greater likelihood of detecting a significant difference.

A ROC curve analysis of the reader data is accomplished by using applications software provided by Charles Metz of the University of Chicago/University of Pittsburgh. The software is operational on a SUN workstation at UVA. Two ROC curves for each reader for each of the six reader questions will be generated, one for the analog mammographic films and one for the digitized mammograms displayed on the grayscale display workstations on our AGFA image display workstation. The index of performance will be the area under the ROC curve for each reader. In the event of a degenerate ROC curve, we analyzed the data using two approaches. One approach utilized the Wilcoxon statistic to estimate the area underneath the ROC curve and the standard error. The second approach involved a third-order spline curve-fitting software program implemented at the University of Virginia.

MAMMOGRAPHY GRAYSCALE READING WORKSTATION

The grayscale workstation for the project is a AGFA review station (IMPAX, RS3000, Ridgefield NJ) which is comprised of a SUN Ultra 2 with 192 Mbytes of RAM, 4 Gbytes of internal HD storage, two DOME high-resolution video cards, and two high-resolution (2k x 2.5k) Orwin grayscale monitors. The system is running Solaris 2.5, with Common Desktop Environment installed and uses the Motif Graphical User Interface. The Review station software is DICOM 3.0 compliant.

We added a Radion 4Gbyte external hard disk drive for storing images from the current reading set, and a Pinnacle Micro Vertex 2.3 Gbyte Magneto-Optical drive as a transfer/backup device.

A separate instance of the SMV software was started on the desktop of each monitor, and expanded to full screen. This allowed two images to be displayed at once. Initially, the LMLO image was displayed on the left monitor, and the RMLO was displayed on the right monitor. This was followed by the LCC and the RCC, respectively, and then images were displayed as requested by the radiologist reader.

DISPLAY WORKSTATION SOFTWARE

The software being used is SMV, a program written by Prof Marty Stanton of Brandeis University. Originally designed for crystallography work, Prof Stanton adapted it to the needs of the Telemammography project by giving it the ability to directly read the images created by the Lumisys 150 laser film digitizer. This made it possible to display the images without going through the intermediate step of converting our data to the DICOM format needed by the IMPAX database of the AGFA review station.

SMV supports all of the image processing techniques needed for the display of the mammography images, including panning, zooming, window-leveling, and grayscale inverting. It also provides features that were used extensively to prepare the images for display, particularly

rotation and cropping.

Two factors had to be considered when preparing the images for display. One was that patient information recorded on the mammography film, as well as indication of the source hospital for the films, had to be masked. The other was that a reduction in the overall size of the images was desirable, to decrease storage requirements and reduce the amount of time required to load and display the image. To address both of these concerns, SMV's cropping feature was used to reduce the image to just the part of the film that actually held the image of the breast. This greatly improved performance of the system, as well as satisfying the protocol requirement that no patient or hospital information be visible to the reader.

DISPLAY PROTOCOLS FOR WORKSTATION

The Display Protocol for the AGFA workstation consists of four displays: Display A (LMLO on left screen and RMLO on right screen); Display B (LCC on left screen and RCC on right screen); Display C (LMLO on left screen and LCC on right screen); and Display D (RMLO on left screen and RCC on right screen). Display A and B were presented to the reader and if requested then Display C and Display D were also presented.

FUTURE EFFORTS

During the Fourth Year of the Contract, we will accomplish the following:

1. Complete reading the 400 cases on the AGFA grayscale workstations
2. Complete the ROC analysis, comparing screen-film readings with those of the grayscale (softcopy) for all 12 readers
3. Complete the NASA ACTS Telemammography readings
4. Complete and evaluate the Wide Area Network connection between Stony Point and MCV and testing the link with the 400 digitized film images. We plan to use a T1 and a FRAME RELAY connection.
5. Complete the Throughput Workflow Analysis

NASA-LERC ACTS TELEMAMMOGRAPHY PROJECT

The ACTS telemammography project a joint effort between NASA's Lewis Research Center, the Cleveland Clinic, and the University of Virginia Department of Radiology. ACTS is NASA's Advanced Communications Technology Satellite. Earth stations have been installed at the three locations. Unix workstations are connected to the earth stations at each location. The purpose of the project is to test the efficacy of using a satellite link as a means of transmitting

mammography images to distant locations. The experimenters are transmitting digitized mammography images via ACTS satellite between UVA, NASA-LERC and the Cleveland Clinic with various techniques and levels of compression. Radiologists at Cleveland Clinic are examining the images to determine their quality and diagnostic effectiveness. The current phase of this project is expected to run through the spring of 1998.

THROUGHPUT ANALYSIS

The performance metrics being used in our Telemammography modeling are diagnostic accuracy and throughput. Diagnostic accuracy is obtained by a ROC analysis. The area under the ROC curve is the probability of correctly distinguishing - on the basis of the diagnostic test results alone - a randomly selected disease case from a randomly selected non-diseased case. Throughput is defined as the rate (jobs-per-minute) at which requests can be serviced by the system. The throughput of a system generally increases as the load on the system initially increases, without the addition of more resources; after a certain load, the throughput stops increasing due to one or more bottlenecks. Throughput analysis is accomplished by listing the resources used and the steps required to complete one job together with the average time per step. The resource with the smallest jobs-per-minute over the complete job, is termed the bottleneck resource.

Table 1 and Table 2 are the resource utilization tables used for conducting throughput analysis, generated for MCV (Medical College of Virginia) and Stony Point (an MCV outpatient clinic), both in the Breast Imaging section of the Department. The resources being modeled in Table 1 and Table 2 are: The Clerk, the Technologist, the Imaging modality, the Film Processor, the File Room, the Resident, and the Radiologist. At each step, the average time to complete the step is measured (minutes). The Throughput for each resource is calculated and recorded at the bottom of each table. For example, in Table 1, the throughput of the Tech is calculated by $1/(13.2 + 4.7 + 1.6 + 5.13) = 0.041$ jobs-per-minute. This calculation assumes that the Tech is working at 100% capacity and can work no faster. In Table 1, the system bottleneck is the Tech since 0.041 jobs-per-minute is the smallest throughput. Likewise, in Table 2, the Tech is again the bottleneck at 0.071 jobs-per-minute.

One of the tasks to be accomplished is the use of modeling techniques for a regional telemammography system. This section of our report describes the modeling schemes we have developed.

INTRODUCTION

Mammography is used routinely to screen for occult breast cancer and is an essential element in the health care service for adult women. Screening mammography is a high volume radiographic procedure with less than one-percent of the cases demonstrating breast cancer. Yet, in retrospect, radiologists do not detect all cancers visible on the radiographic images. Missed detections are due to such factors as low conspicuity of the lesion, poor image quality,

radiologists' fatigue, and oversights by the radiologists (1). Screen-film mammography is the imaging modality most often used (2-5), but Full Breast Digital Mammography (FBDM) is current printers are limited to printing arrays of only 4k X 5K x 12 bit on 8 X 10 or 10 X 12 inch detection, high contrast resolution over a large dynamic range, and high detector quantum efficiencies for x-rays. The digital technology of FBDMs also provides the capability to separate and optimize the functions of image generation and image display. In addition, FBDM systems offer improved access to digital technology, with its promise of inexpensive telemammography and of using newly developing digital data management systems. The challenge for FBDM systems is managing and displaying the extremely large amount of digital image data generated. These systems generate a 4800 x 6400 x 14-bit digital array per image. The data per screening examination is 215 Mbytes for four standard screening views (craniocaudal (CC) view, left and right breast; mediolateral oblique view (MLO), left and right breast). In comparing the new examination to the previous examinations, a total of over 430 Mbytes of image data needs to be displayed efficiently. Two choices for display technologies are: (a) high resolution laser film printers; and (b) interactive grayscale workstations.

The limitations regarding the choice for FBDM image display are significant. Laser film printers are difficult to utilize because optimized look-up tables for each image are needed and current printers are limited to printing arrays of only 4k x 5K x 12 bit on 8 x 10 or 10 x 12 inch film. On the other hand, interactive grayscale workstations display only a 2k x 2.5k at 8/12 bits (12 bits from a frame buffer) per monitor, require complex display protocols (display and peregrinating through 8 images, each 6.4k x 4.8k x 12 bits, viewed by a 2k x 2.5k display screen per monitor). The usual choice, due to cost, is two monitors per workstation. Thus there are tradeoffs between these two display technologies.

The advantages of the high resolution laser film printer are the following: (a) the matrix size of the laser printed digital mammography images (5k x 4k) comes close to matching that of the FBDM image (6.4k x 4.8k); (b) the size of the laser film printed image matches that of the screen-film size of 8 x 10 or 10 x 12 inches and (c) once printed and processed, the laser film printed image can be displayed on mammography view boxes and managed in the same manner as are standard screen-film images. The disadvantages of the laser film printer are the following: (a) requires 20 seconds per image for exposing the latent image (prints 1 line per 2.2 msec) and then the standard 90 seconds to develop the film before clinical interpretation of each image is possible; (b) look-up tables must be developed to compensate for nonlinear optical characteristics of film; in addition, because the dynamic range of film (optical density from 0.2 up to 3.0 or less) is much less than that of digital mammographic detectors, dynamic range compression algorithms and/or multiple films per image are often required; (c) the FBDM creates images with up to 14 bits, while the laser printer prints 8-bit or 12-bit images according to its look-up tables; and (d) the laser film printed image cannot be interactively adjusted for such image enhancement as window and level settings. No study has been conducted in developing the best parameters for the use of laser printed films for FBDM.

The advantages of the interactive grayscale workstation are the following (a) the ability to

interactively modify the display image throughout the 12 bit range (window-level, zoom image processing, computer-aided diagnosis algorithms); (b) the use of multiple displays for comparing images (current and previous examinations); (c) rapid retrieval and display from the archiving storage; and (d) design and use of individual display protocols. The disadvantages of the interactive grayscale workstation for digital mammography are the following: (a) it is only possible to view a 2k x 2.5k portion of the full resolution FBDM image; (b) sub-sampling or binning is required to display the full-size digital mammography image; (c) multiple monitors are required for each interactive workstation to display the two CC views and the two MLO views; and (d) user throughput is dependent on reader facility with the workstation interactive functions. No studies have been conducted to determine the best parameters for an interactive FBDM grayscale workstation.

Models of individual clinical observations permit predicting future impact of new technologies under study. A stochastic model for the general theory of screening for early detection of breast cancer was first presented by Eddy (9). His model utilized the metrics of sensitivity and prognosis as a function of early detection. His work provided a time-varying Markov Chain (10) and methods for estimating the probability transitions between the states of the model. Others (11-13) have added to the information concerning stochastic breast cancer screening methods, modeling the disease and its detection via one of more diagnostic examinations. There exists a need to develop a screening model that will incorporate the FBDM technology and the operational parameters of display technology, together with the metrics of diagnostic accuracy and throughput-to-cost-ratio. Diagnostic accuracy determines how well a screening mammography examination is used for detection of breast cancer. Throughput is the rate at which mammography examinations can be completed. The cost of a digital mammography examination is calculated from the resources used to complete the examination. The throughput-to-cost-ratio is a metric by which we can measure the cost of achieving a selected throughput. No stochastic screening model has been implemented which utilizes the metrics of diagnostic accuracy and throughput-to-cost-ratio in optimizing display protocols for FBDM systems.

Models, due to their assumptions, have restrictions placed upon the variables being modeled. Such models require estimation only of the parameters assumed by the model. This reduces the required sample sizes. However, concern exists regarding the model errors (all models are in error). The use of a model requires some level of validation or experimental justification.

MODELING

A good model of an examination will predict the usefulness of the exam. The parameters of the model will have to be estimated. A good model will reduce the data required to determine diagnostic accuracy, throughput, and cost.

1. ROC Analysis

Analysis is based upon a two-by-two contingency table (Figure 1). The symbols are: ab is abnormal and nl is normal; AB is normal and NL is normal. We note that $P(AB/ab) + P(NL/ab) = 1$ and that $P(AB/nl) + P(NL/nl) = 1$. Thus, of the four conditional probabilities, two of them are linearly independent. An ROC analysis is conducted by estimating two conditional probabilities, based upon an observation variable (Figure 2). The ROC graph (Figure 3) is generated by moving the value of the decision threshold, X_c across the range of the observational variable X_p .

The steps in conducting an ROC analysis are well known (14-21). The 2×2 contingency table is carefully defined. A statistical power is initially selected and the number of samples and readers are calculated. The number of samples (cases) are selected so that one-third are very difficult to read, one-third are very hard to read, and one-third are fairly hard to read. A 5-point multiscale reading is performed on each case by each reader for specific image features. There are a number of available ROC software programs that will process the multiscale reading data to provide the ROC graph. The area under each reader's ROC graph is the index of performance (the probability that a random selected patient undergoing the results of the examination will be a correct true-positive).

The advantages of ROC analysis are several. It is a well-known tool, often used by radiologists. Software exists which will generate the ROC graph from multi-scale readings by each reader. The area under the ROC graph is used as an index of reader performance. The disadvantages of ROC analysis is that it remains a binary decision model. It is difficult to incorporate population statistics (a priori). The ROC analysis is sensitive to modifying the readers or cases.

2. Matrix Modeling

A binary examination described by a two-by-two contingency table may be placed into a matrix model (Figure 4). The binary decision model as illustrated has two input states (normal, abnormal) and two output states (normal, abnormal). The advantage of the matrix representation is the useful manipulation of the matrices in describing probabilistic outcomes of multiple examinations. For example, Figure 5 illustrates the results of cascading two examinations while Figure 6 illustrates a decision tree model of the two cascaded examinations. The results of cascading two examinations show that the resultant transition probabilities are less than that of each individual examination - a result sometimes called "leading information." In Figure 6, the a priori probabilities are $P(1)$ and $P(2)$. For example $P(7/1)$ is given by: $P(7/1) = P_{13}P_{57} + P_{14}P_{67} = P_{17}$.

A model of double reading is illustrated in Figure 7. In double reading, reader 1 and reader 2 independently read the results of the examination. They then compare their outcomes using a decision rule. Table 1 defines the set of possible reader outcomes for each reader. Tables 2 and 3 provide a decision rule that defines the conditions under which the readers are said to be equal or different. A more conservative decision rule would be to say that the two readers are equal if they achieve identical outcomes and that the two readers are different if they do not have

identical outcomes. It is believed by some researchers that computer aided decision algorithms could serve as a partial second reader.

The sequence of outcomes from the decision rule, based upon the results of both readers, can be assumed to be an n -sequence of the symbol set $(0,1)$ where the alphabet symbol of "0" means equal results and the alphabet symbol of "1" means different results from the two readers. If these results are observed for a very long time, the sequence of symbols (with probability one) will be "typical." That is, the resultant sequence of outcomes from the decision rule is ergodic. This implies that a n -sequence of outcomes, as n increases, will result in typical sequences (those close to the expected value) and the rest being non-typical (those with probabilities approaching zero as n increases)

3. Uncertainty Modeling

Uncertainty modeling is a probabilistic scheme (Figure 8) in which there is a sequence of trials (say n) and conclusions are drawn on the resultant n -sequences being close to there expected values (22). The concept of *typical sequence*, as introduced by Wolfowitz (23), who called them X sequences, and as used by Ash (24), is related to the asymptotic behavior of its independent, identically distributed random variables (25-28). Let Y be the random variable taking on the values of (y_1, y_2) (for the outcome of the FBDM test) or $(y_1, y_2, y_3, y_4, y_5)$ (for the outcome of the readers from a multiscale reading, respectively). Suppose that the experiment associated with Y is performed " n " times. That is, a sequence will be generated of Y_1, Y_2, \dots, Y_n of independent, identically distributed random variables, each having the same probability distribution as Y . If we define a function $f_i = f_i(Y_1, Y_2, \dots, Y_n)$ to be the number of times the symbol y_i occurs in the sequence Y_1, Y_2, \dots, Y_n , then y_i will f_i has a binomial distribution with parameters n and p_i . We identify a "typical" sequence as those sequences in which f_i is "close" to np_i for every i where np_i is the number of times that the expected value of y_i will occur in the n -sequence. Then we note that the set of nontypical sequences has a small probability of occurrence. Thus in a typical sequence, each symbol y_i occurs approximately with its expected frequency of np_i . The formal definition is the following. Given $c > 0$, choose any positive number k such that $1/k^2 < c/M$ where M is the number of symbols or values that the random variable Y takes on. Let $b = (b_1, b_2, \dots, b_n)$ be a sequence of symbols, each b_i being one of the symbols of the set (Y_1, Y_2, \dots, Y_m) . We say the sequence b is typical if

$$|f_i(b) - np_i| / \sqrt{np_i(1-p_i)} < k$$

It can be shown that the following is true: (a) the set of nontypical sequences of length " n " has a total probability $< c$; and (b) the number of typical sequences of length " n " is $2^{n(H + r_n)}$, where r_n approaches zero exponentially as n grows large and (c),

$$H = (f_1(b) \log p_1 + f_2(b) \log p_2 + \dots + f_M(b) \log p_m)$$

If the output symbols are X_1, X_2, \dots, X_M , and the out symbols are y_1, y_2, \dots, y_L and the transition probabilities are $[a_{ij}]$, where $a_{ij} = P(y_j/x_i)$, $i = 1, \dots, M$ and $j = 1, \dots, L$, then the joint distribution of the input X and output Y is given by

$$P(X = x_j, Y = y_j) = P(x_i)P(y_j/x_i), i = 1, 2, \dots, M, \text{ and } j = 1, 2, \dots, L$$

and the distribution of Y is given by

$$P(y_j) = P(X_1)P(y_j/x_1) + P(x_2)P(y_j/x_2) + \dots + P(x_M)P(y_j/x_M).$$

For $M=2$ and $L=5$, then $P(Y = y_j) = P(x_1)P(y_j/x_1) + P(x_2)P(y_j/x_2)$, $j = 1, \dots, 5$. If the experiment is repeated "n" times, then if $b = (b_1, b_2, \dots, b_n)$ is a sequence of resultant n-symbols, each b_i being one of the elements (y_1, y_2, \dots, y_5) , then we say that the n-sequence is typical if it satisfies the above definition.

The significance of the use of *typical sequences* is in analyzing the model of the diagnostic test and reader responses. Typical sequences reduce the number of n-sequences that require analysis. For a large n (number of independent trials), there are approximately $2^{nH(X)}$ typical input n-sequences, each with probability roughly $2^{-nH(X)}$. Similarly there are $2^{nH(Y)}$ typical output n-sequences and $2^{nH(X,Y)}$ typical pairs of input and output n-sequences. A typical pair may be generated by first selecting a typical output n-sequence y and then selecting a typical input n-sequence x such that (x,y) is a typical pair. Since the number of typical output sequences is $2^{nH(Y)}$ and the number of typical pairs is $2^{nH(X,Y)}$, then for each typical output sequence y, there are

$$2^{nH(X,Y)-nH(Y)} = 2^{nH(X/Y)}$$

input sequences x such that (x,y) is a typical pair. That is, if a typical sequence y is presented then the number of typical input sequences possible are approximately $2^{nH(X/Y)}$ (not $2^{nH(X)}$) each with approximately the same probability, $2^{-nH(X/Y)}$. This is important since it reduces the number of n-sequences that are to be analyzed. Hence, if the experiment is conducted say 100 times ($n=100$ or reading out 100 cases) then we can expect approximately $2^{100H(X/Y)}$ typical sequences, each with approximate probability of $2^{-100H(X/Y)}$. It is known that, given the transition probabilities (such as obtained from an ROC analysis), then by varying the input distribution $P(X)$, one can obtain a maximum of the mutual information, $I(X;Y) = H(X) + (H(Y) - H(X/Y))$, between the input, X, and the output, Y, which is called the channel capacity, C. Hence, given the transition probabilities between input and output, (P_{ij}) , there exists an input distribution $P(X)$ such that the mutual information between X and Y, $I(X;Y)$, is a maximum. The result suggests that for a given input distribution $P(X)$, the *a priori* distribution, the transition probabilities may be changed to better approach the channel capacity, C.

If we are modeling an examination, then Figure 9 illustrates the relations between different uncertainty measures. These measures are given by:

$$H(X) = -\sum P_i \log P_i$$

$$H(Y) = -\sum P_j \log P_j$$

and

$$H(X,Y) = -\sum_i \sum_j P(X_i, Y_j) \log P(X_i, Y_j)$$

The mutual information between (X,Y) is given by

$$\begin{aligned} I(X;Y) &= H(X) - H(X/Y) \\ &= \sum_i \sum_j P(X_i, Y_j) \log \frac{P(X_i, Y_j)}{P(X_i)} \end{aligned}$$

$$= \sum_i \sum_j P(X_i, Y_j) \log \frac{P(X_i, Y_j)}{P(X_i) P(Y_j)}$$

Figure 9 illustrates a graphical schematic of these relationships.

Figure 10 is a model of double reading as previously cited. We are interested in the mutual information, $I(A; B, C, D, E)$. This is the mutual information regarding "A" on condition of the occurrence of (B, C, D, E). It is given by:

$$\begin{aligned} I(A; B, C, D, E) = & I(A/C) + I(A; B/C) \\ & + I(A; D/B) + I(A; D/C) \\ & + I(A; E/B) + I(A; E/C) \\ & + I(A; E/D). \end{aligned}$$

The conditional mutual information terms, such as $I(A; D/C)$, is the average amount of information about the set "A" provided by an observation from the set "D" after an observation from the set "C".

Figure 11 is a model for display protocols (either laser printed film or soft copy, the grayscale workstation) for digital mammography. Then the occurrence of (B, C, D, E, F, G) that tells us about the set "A" is the following:

$$\begin{aligned} I(A; B, C, D, E, F, G) = & I(A; C) + I(A; B/C) \\ & + I(A; D/B) + I(A; D/C) + I(A; E/B) \\ & + I(A; E/C) + I(A; E/D) + I(A; F/B) \\ & + I(A; F/C) + I(A; F/D) + I(A; F/E) \\ & + I(A; G/B) + I(A; G/C) + I(A; G/D) \\ & + I(A; G/E) + I(A; G/F). \end{aligned}$$

The necessary parameters for this model are conditional probabilities. The value of $I(A; B, C, D, E, F, G)$ tells us the number of typical sequences in an n-sequence as well as their probability of occurrence. The decomposition of $I(A; B, C, D, E, F, G)$ into simpler terms, such as $I(A; G/F)$ provides for a much simpler model.

THROUGHPUT ANALYSIS

The three techniques for performance measurement of a system are analytical modeling, simulation, and measurement of an actual system (29). The major consideration in deciding which evaluation technique to use is the life-cycle stage in which the system resides. Measurements are possible if technology similar to the system being evaluated already exists. If the system under study is new, then only analytical modeling and simulation methods are possible. Simulation is difficult and time-consuming to accomplish. For the mammography systems, the only reasonable evaluation technique is analytical modeling. The performance metrics being used in our modeling of these systems are throughput and diagnostic accuracy. Throughput is defined as the rate (jobs-per-minute) at which requests can be serviced by the system. The throughput of a system generally increases as the load on the system initially increases, without the addition of more resources; after a certain load, the throughput stops increasing due to one or more bottlenecks. Throughput analysis is accomplished by listing the

resources used and the steps required to complete one job. The resource with the highest total service demand has the highest utilization and is called the bottleneck resource. The area under the ROC curve (14) is the probability of correctly distinguishing - on the basis of the diagnostic test results alone - a randomly selected disease case from a randomly selected non-diseased case.

Table 4 and table 5 (30) are the resource utilization tables generated for two throughput and bottleneck analyses. The top row of each table lists the resources being modeled. The rows of tables are the steps required to complete one reading. The bottom rows (throughput per minute) are generated by alternately assuming that each resource in the columns is operating as rapidly as it possibly can.

The bottleneck analysis described above is based on Little's Law (31) of mean value queuing analysis. Little's Law states that the mean number of jobs in a system equals the mean throughput rate multiplied by the mean time in the system. We have conducted similar studies for screen-film mammography. Table r (labeled "MCV") is a Resource Utilization table for mammography at the Medical College of Virginia (provided by Dr. Ellen Shaw de Paredes) and Table 5 (labeled "SP") is for an outpatient Breast Imaging Center.

The throughput analysis is conducted by obtaining the upper and lower bound (Figure 12) on the actual throughput as a function of one or more of the resources. Upper and lower bounds are required to understand the otherwise complex analysis of the actual throughput. If the radiologist is selected as the independent variable (increasing the number of radiologists), then the upper bound on the throughput is given by

$$\text{Upper Bound} = \min[1/T_{\text{sys}}, N/(T_{\text{sys}} + T_{\text{reader}})]$$

where T_{sys} is the time used by the system less the radiologist and resident time and T_{reader} is the time used by the radiologist and the resident reading out the cases (while system is waiting). Then $1/T_{\text{sys}}$ is the maximum throughput. The term $N/(T_{\text{sys}} + T_{\text{reader}})$ relating increases in the number of radiologists (and residents) increases linearly with N until it reaches $1/T_{\text{sys}}$, after which the system cannot increase its throughput no matter how many radiologists (and residents) are added to the reading room. This is the case when the radiologist is unable to do any other work above the throughput limit because the system is then queuing examinations. We note that as N increases (N could be other resources such as technologists), then there is a method for calculating the lower bound on the throughput. That is,

$$\text{Lower Bound of Throughput} = N/(NT_{\text{sys}} + T_{\text{reader}}).$$

This will occur when the system is busy doing other things and the newest case is last in the queue to receive service. Figure 22 illustrates this analysis of throughput.

SUMMARY

We have reviewed modeling of mammography examinations. Modeling is essential due to the large number of variables. However, a carefully selected model will require only the estimation of the model parameters. Of the models we have described, the uncertainty modeling

is superior owing to its restrained relationships and requiring only the estimation of conditional probabilities. The throughput analysis is a method that is simple to utilize in estimating workflow.

CONCLUSIONS

The following conclusions regarding the Telemammography research project have been reached:

1. Collection of the 400 mammography screen-film database is critical to the project.
2. The grayscale workstation must be carefully implemented to perform a ROC softcopy analysis. Critical elements are the following:
 - a. Needed software to obtain an acceptable display protocol.
 - b. Required disc and ROM space to archive four 4k x 4k x 12 bit images.
 - c. Need CD-ROM to archive 50 cases for each reader session.
 - d. Need display software that will provide the ability to read 40 cases per hour.
3. Conclusions regarding an adequate wide-area-network await completion of the fourth year of the project. The following are being tested.
 1. TI Link.
 - b. ISDN Link.
 - c. FRAME RELAY Link.
 - d. Satellite Link.

LAY PUBLIC ABSTRACT

Telemammography is the transmission and interpretation of digitized mammographic images. The use of telemammography will allow for interpretation of on-site mammograms from distant areas by expert radiologists at a central site. This can potentially increase the access to mammography for many women.

We are testing a telemammography system utilizing digitized mammograms that are transmitted through telephone lines or satellites and are interpreted on computer workstations. The goal of this study is to determine the requirements to deliver high quality mammographic images from remote locations.

To test the system we have collected 400 normal and abnormal mammograms which have been interpreted by 12 radiologists. The radiologists are interpreting the studies on film as well as computer workstations, and we are comparing their accuracy with two methods.

We also are assessing the performance of the system by comparing the patient workflow when their mammograms are performed using routine mammographic film versus digitized mammograms.

We have found that reading mammograms on the workstations versus on film reduces the patient throughput. Also because of the decreased brightness of images on the workstations versus viewing films on traditional light boxes, the display of some images is difficult.

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		Output	
		AB	NL
Input	ab	P(AB/ab) True positive	P(NL/ab) False negative
	nl	P (AB/nl) False positive	P(NL/nl) True negative

Figure 1
Two-By-Two Contingency Table

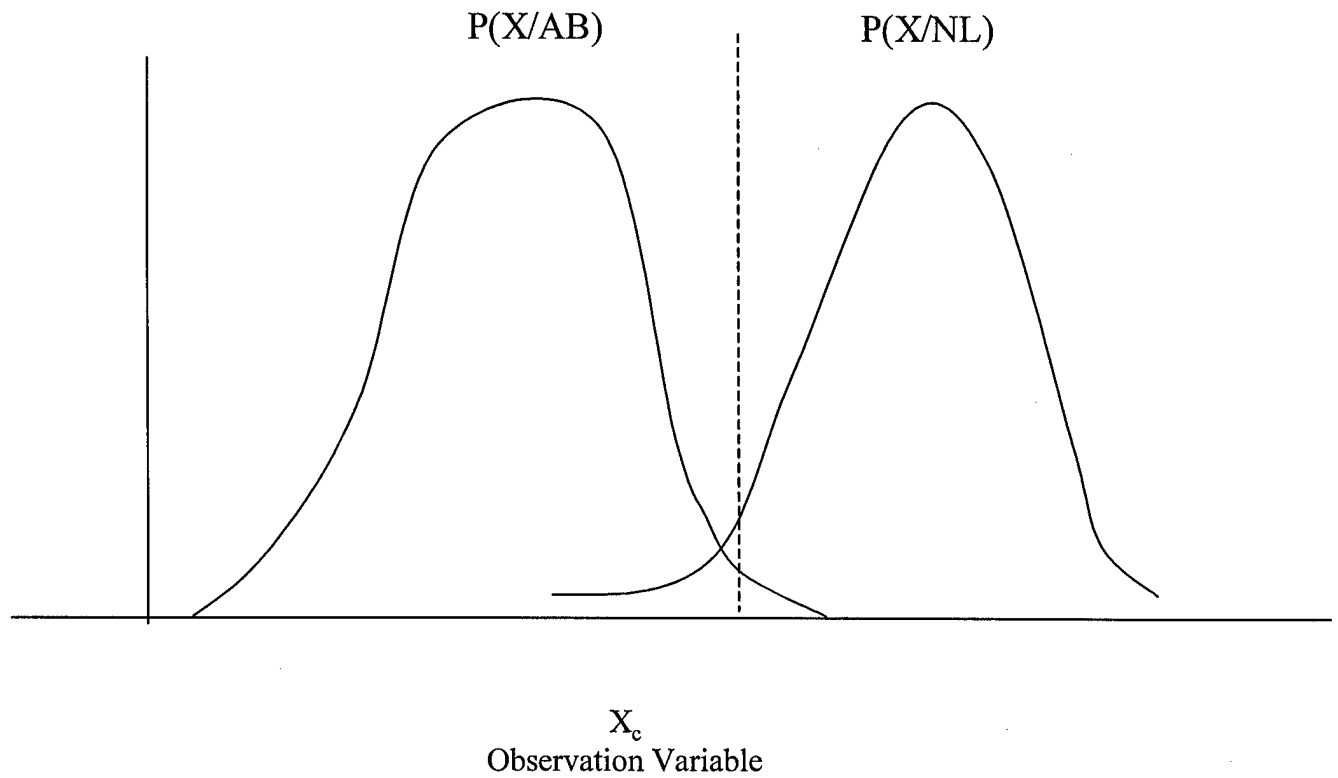


Figure 2

Model of ROC. The value of X_c is moved across the range of the observation variable, generating the ROC graph

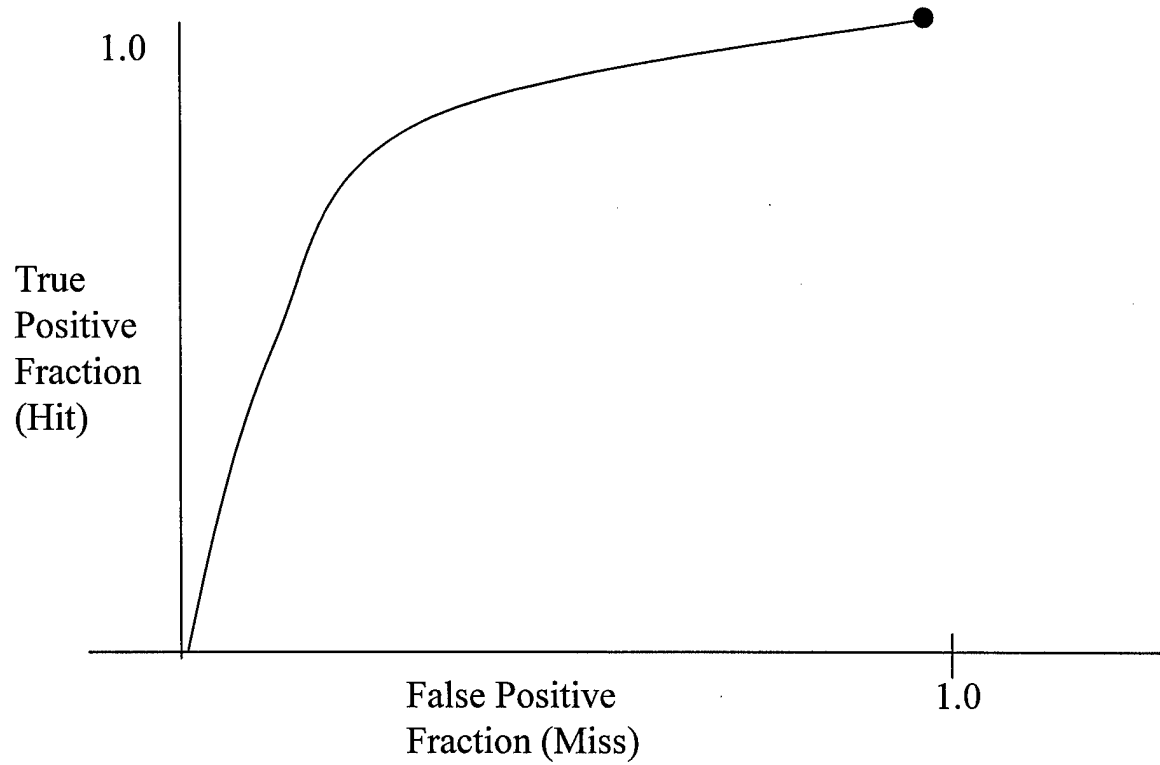
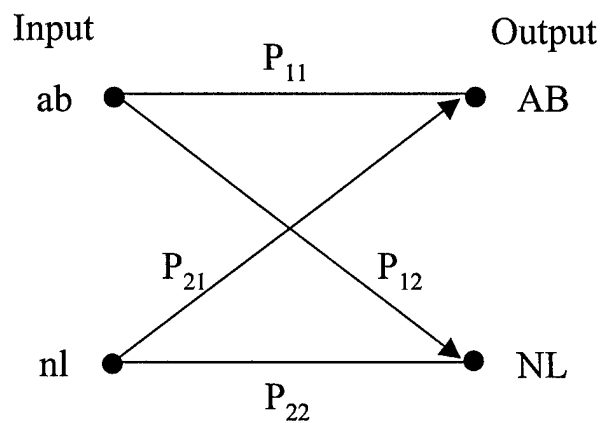


Figure 3
ROC Graph



$$P_{11} = P(AB/ab)$$

$$P_{21} = P(AB/nl)$$

$$P_{12} = P(NL/ab)$$

$$P_{22} = P(NL/nl)$$

$$\begin{bmatrix} P_{11} & P_{12} \\ P_{21} & P_{22} \end{bmatrix}$$

Figure 4
Matrix Modeling
of an Examination

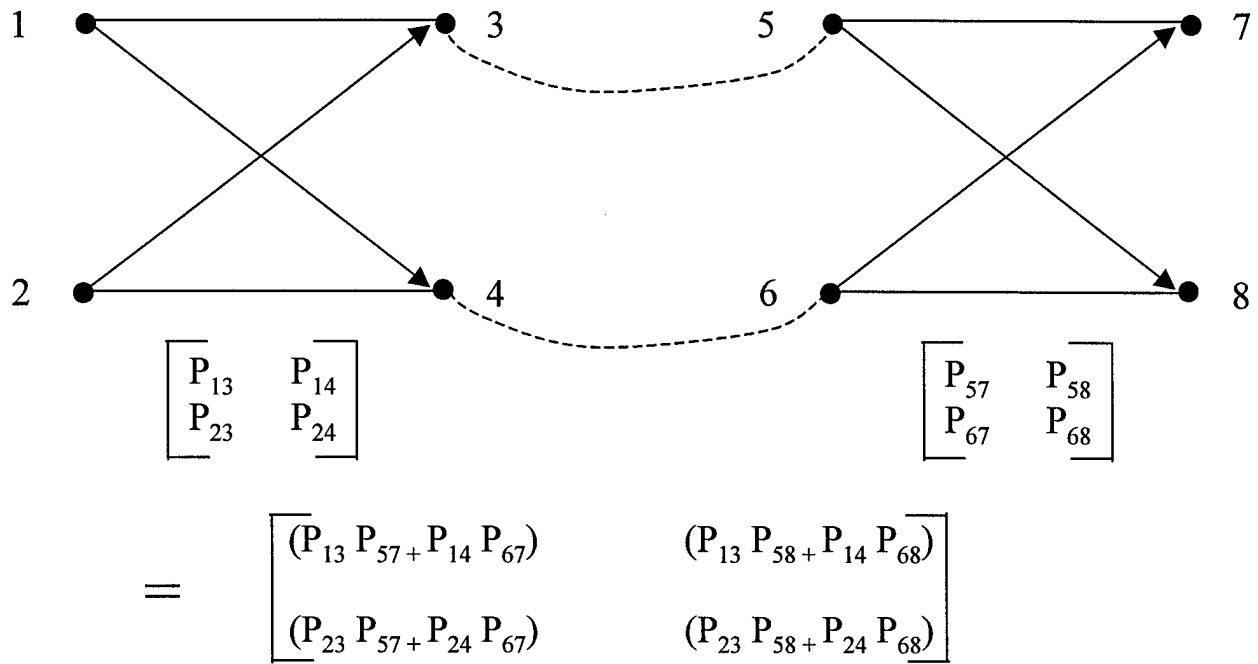


Figure 5
Modeling of Cascaded
Examination

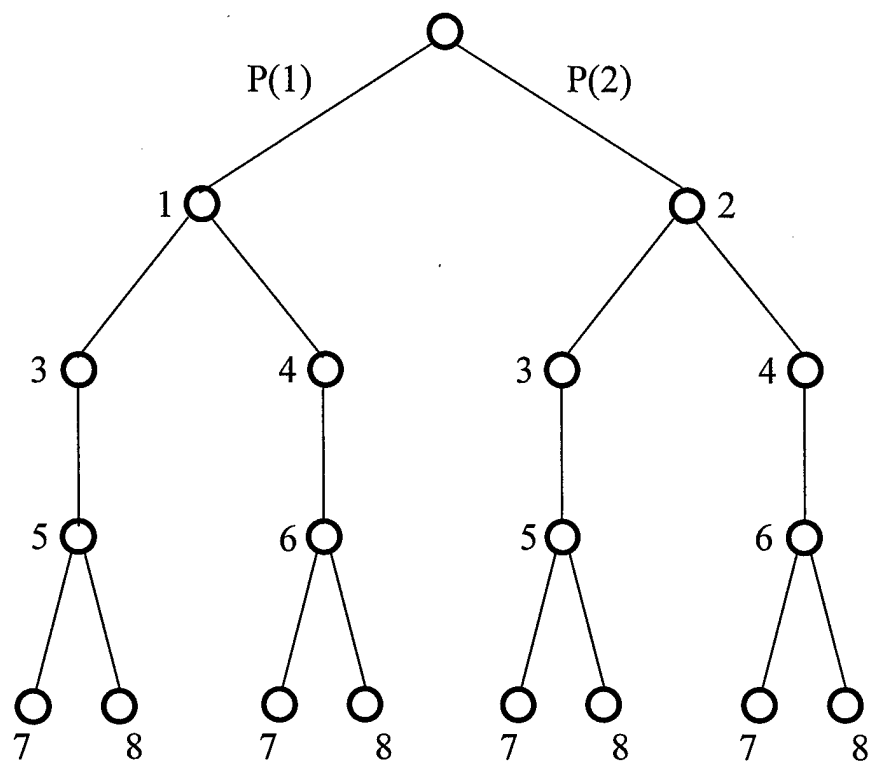


Figure 6
Decision Tree Modeling
of Cascaded Examinations

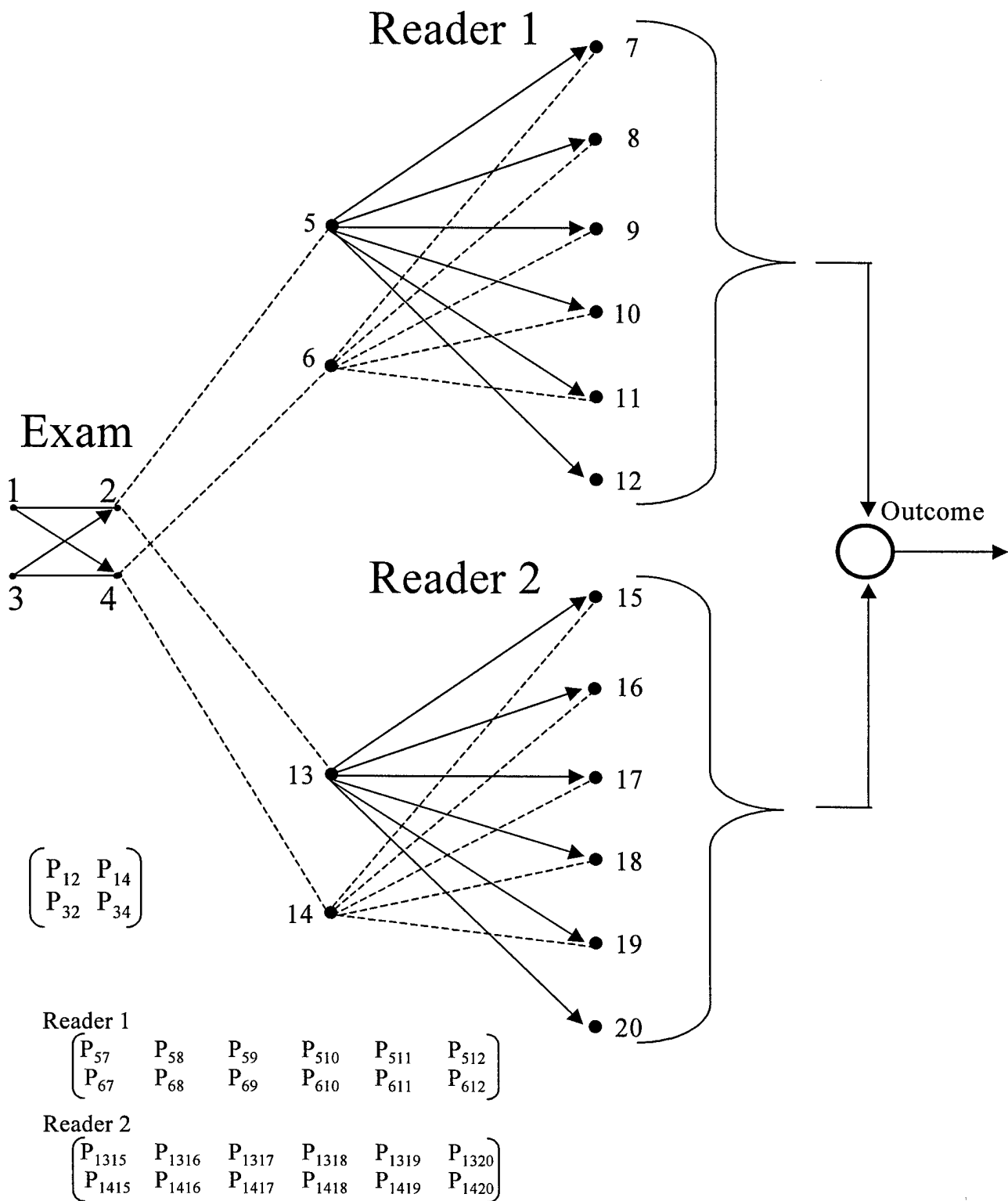


Figure 7
Model of Double Reading

Table I
Reader Outcome for
Modeling of Double Reading

<u>Outcome States</u>	<u>Meaning Assigned</u>
7 or 15	Patient recalled
8 or 16	Patient negative (return 1 year)
9 or 17	Benign findings (return 1 year)
10 or 18	Probably benign (return 6 month)
11 or 19	Suspicious finding (do biopsy)
12 or 20	Malignant, highly suspicious (do biopsy)

Table 2
Decision Rule for Two Readers Outcomes Said to Be Equal

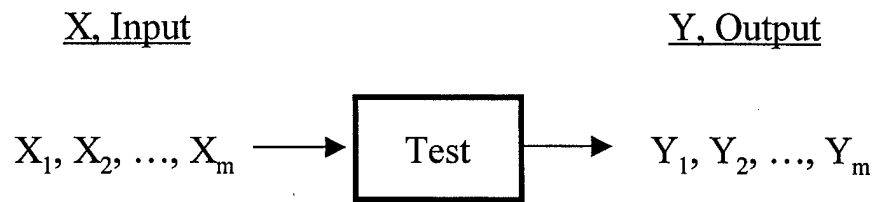
Outcome:

- Negative and benign
- Suspicious and malignant
- Probably benign

Table 3
Decision Rule for Two Readers Outcomes Said to Be Different

Outcome:

- Benign and probably benign
- Probably benign and suspicious finding
- Negative and suspicious finding
- Benign and suspicious
- Negative and malignant
- Benign and malignant
- Probably benign and malignant



$$\begin{aligned}
 & \begin{matrix} H(X) & H(X,Y) & H(Y) \end{matrix} \\
 & I(X;Y) = H(X) - H(X/Y) \\
 & \quad \quad \quad = H(X) = H(Y) - H(X,Y)
 \end{aligned}$$

Figure 8
Uncertainty Measures

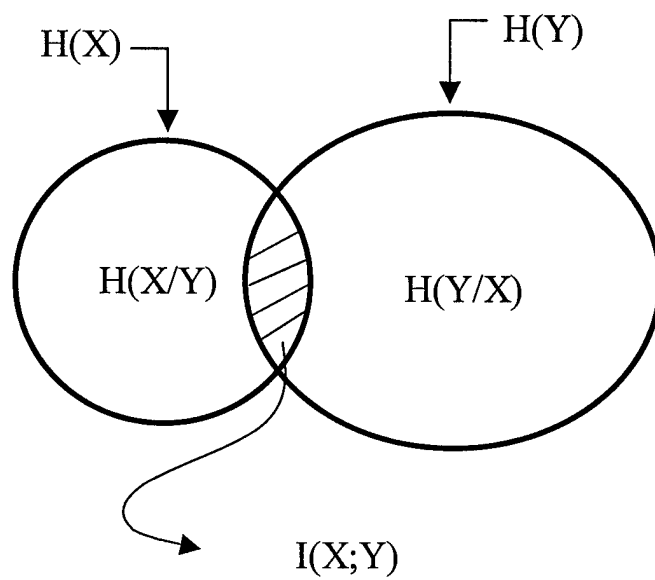


Figure 9
Uncertainty Measures

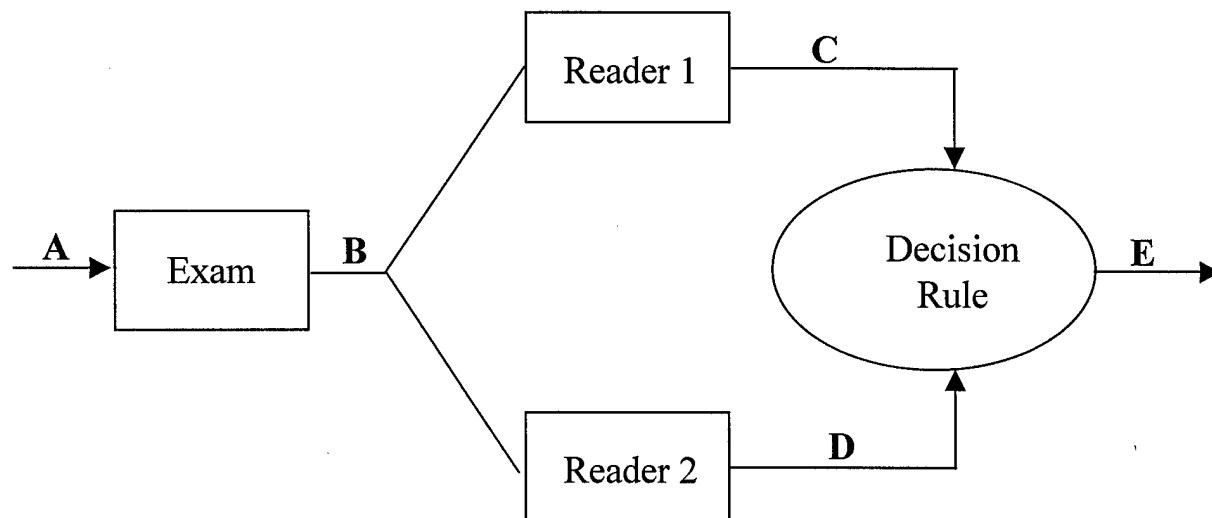


Figure 10
Modeling of Double Reading

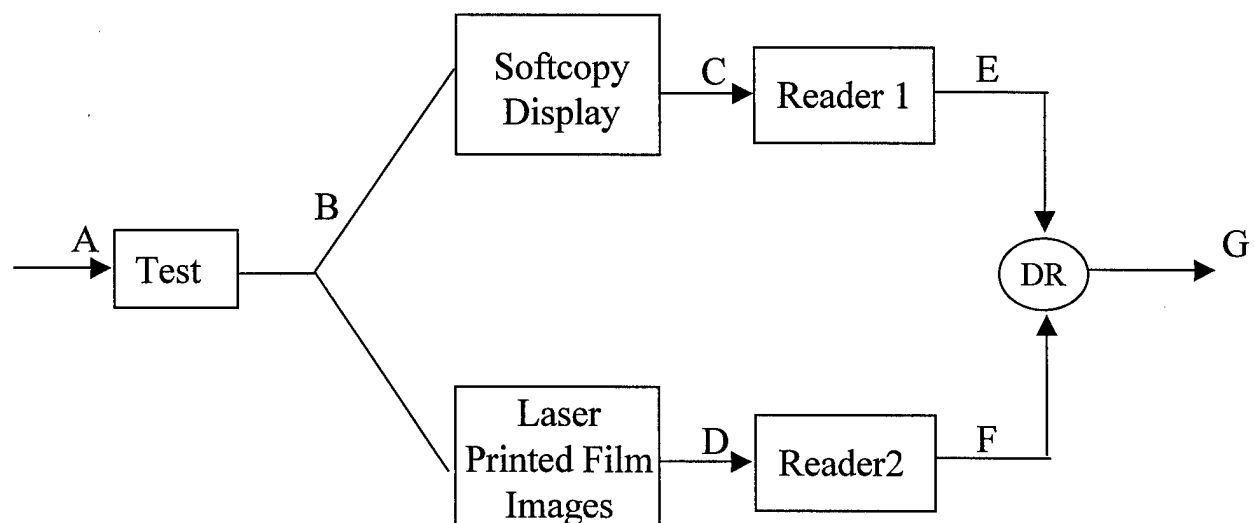
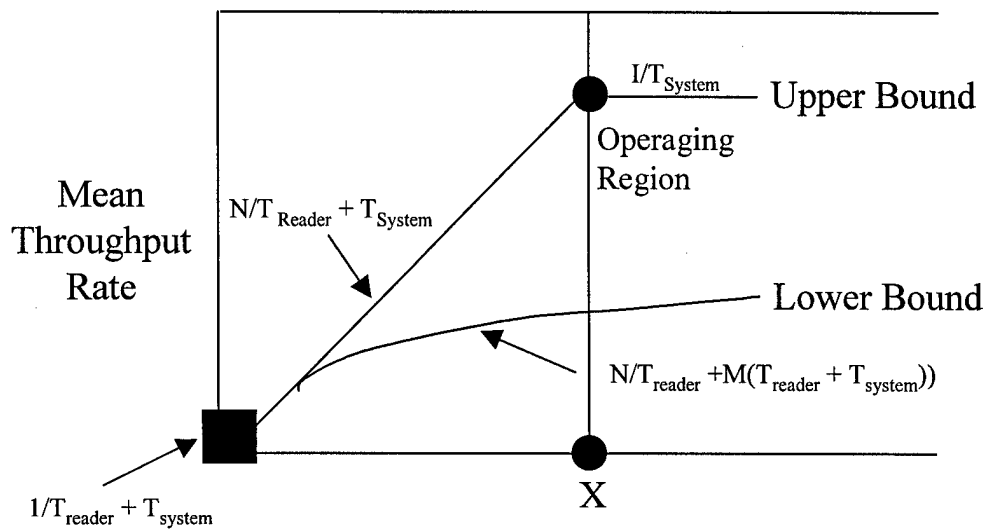


Figure 11
Modeling Display Protocols
for Digital Mammography



Number of Jobs
 $X = (T_{\text{reader}} + T_{\text{system}}) T_{\text{system}}$

Figure 12
 Throughput Analysis

Table 1: MCV

STEP	CLERK	TECH	MODALITY	FILM PROCESSOR	FILM ROOM	RESIDENT	RADIOLOGIST
REGISTRATION	11.5	0	0	0	0	0	0
PRIOR FILM AND/OR FILM RETRIEVAL	0	0	0	0	1.75	0	0
IMAGE ACQUISITION	0	13.2	13.2	0	0	0	0
FILM PROCESSED	0	4.7	0	4.7	0	0	0
QUALITY ASSURANCE	0	1.6	0	0	0	0	0
PRE-ACQUISITION AND PROCESS	0	5.13	5.13	5.13	0	0	0
FILM HUNG	0	0	0	0	0.39	0	0
REVIEW OF CLINICIAN INFORMATION	0	0	0	0	0	0.25	0
FILMS READ	0	0	0	0	0	0.62	0.62
ADDITIONAL VIEWS, STUDIES							
WRITE EARLY READING	0	0	0	0	0	0.34	0
REPORT DICTATION	0	0	0	0	0	1.22	0
NOTIFY CLINICIAN	0	0	0	0	0	1.43	0
REVIEW RESULTS WITH PATIENT	0	0	0	0	0	0	1.34
COMPARISON WITH PRIOR FILM	0	0	0	0	0	0	0.44
DICTATE ADDENDUM TO REPORT	0	0	0	0	0	0	0.81
FILING OF REPORT	0	0	0	0	0.46	0	0
THROUGHPUT	0.067	0.041	0.055	0.102	0.384	0.259	0.311

Bottleneck is the Technologist (0.41 jobs per minute).

Table 2: Stony Point

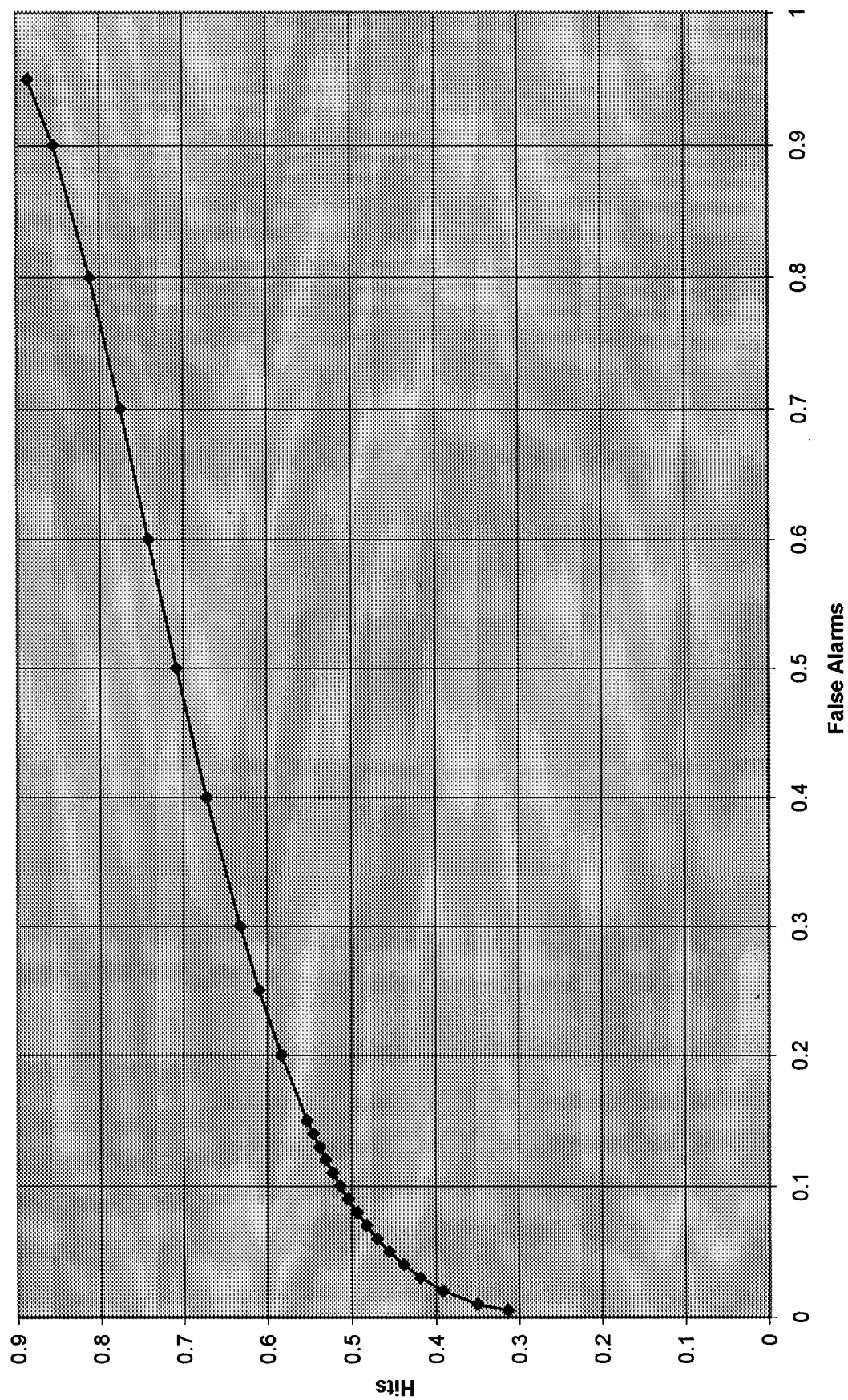
STEP	CLERK	TECH	MODALITY	FILM PROCESSOR	FILM ROOM	RESIDENT	RADIOLOGIST
REGISTRATION	13.6	0	0	0	0	0	0
PRIOR FILM AND/OR FILM RETRIEVAL	0	0	0	0	0.38	0	0
IMAGE ACQUISITION	0	7.3	7.3	0	0	0	0
FILM PROCESSED	0	4.7	0	5	0	0	0
QUALITY ASSURANCE	0	0.48	0	0	0	0	0
PRE-ACQUISITION AND PROCESS	0	1.3	1.3	1.3	0	0	0
FILM HUNG	0	0	0	0	0.52	0	0
REVIEW OF CLINICIAN INFORMATION	0	0	0	0	0	0.3	0
FILMS READ		0	0	0	0	0.96	0.96
ADDITIONAL VIEWS, STUDIES							
WRITE EARLY READING	0	0	0	0	0	0.35	0
REPORT DICTATION	0	0	0	0	0	1.09	0
NOTIFY CLINICIAN	0	0	0	0	0	0.14	0
REVIEW RESULTS WITH PATIENT	0	0	0	0	0	0	0.84
COMPARISON WITH PRIOR FILM	0	0	0	0	0	0	0.63
DICTATE ADDENDUM TO REPORT	0	0	0	0	0	0	0
FILING OF REPORT	0	0	0	0	0.43	0	0
THROUGHPUT	0.074	0.07	0.116	0.159	0.757	0.353	0.412

Bottleneck is the technologist (0.071 jobs per minute)

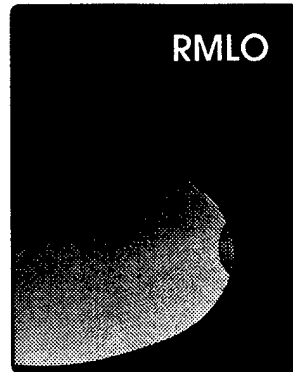
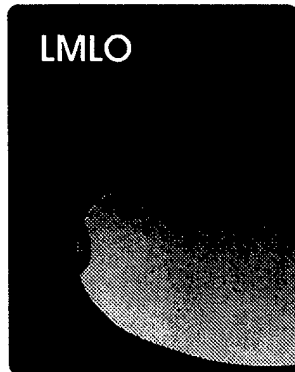
The authors wish to gratefully acknowledge the efforts of the following radiologists who have participated as readers for this project:

Dr. Herman Bosch
Dr. M. Pinson Neal, Jr.
Dr. Karsten Konerding
Dr. Cherie Scheer
Dr. Ronald Robinson
Dr. Thomas Langer
Dr. Gia DeAngelis
Dr. Ruth Moran
Dr. Jennifer Harvey
Dr. Laurie Fajardo
Dr. Jacquelyn Hogge
Dr. Shashank Parekh
Dr. Patricia Buchanan

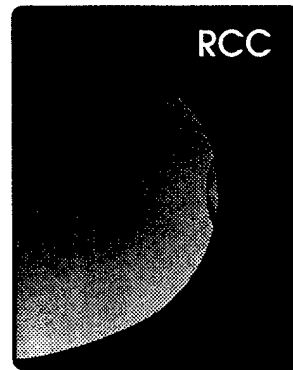
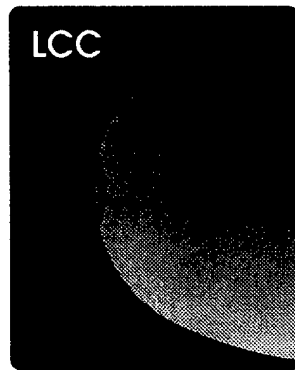
Reader02 Analgo ROC: Type=Calc N=400 Area=.6947 STD Area=.0452



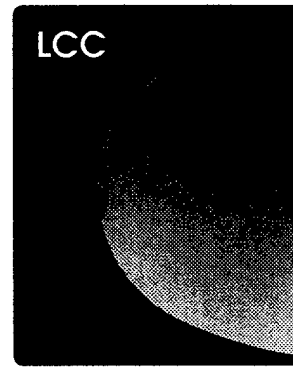
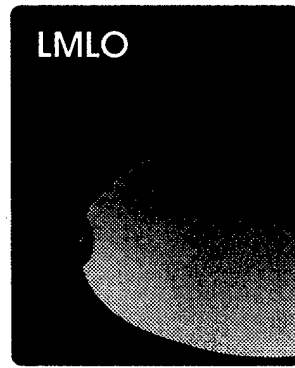
DISPLAY PROTOCOLS



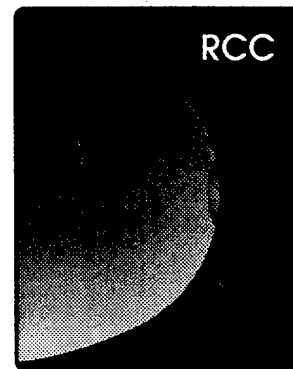
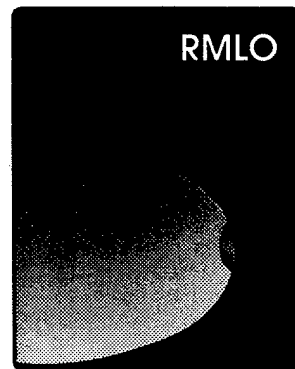
Display A



Display B

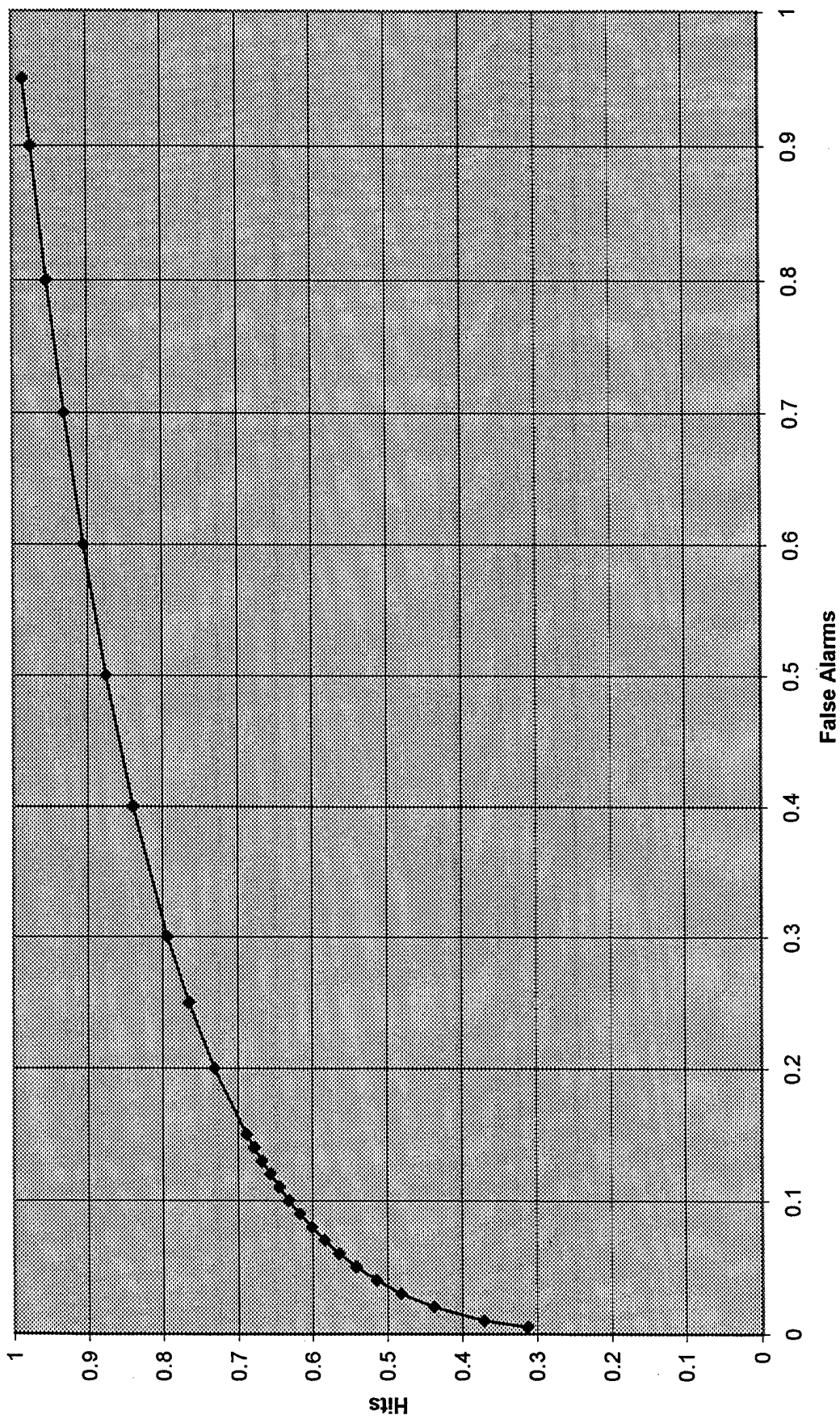


Display C

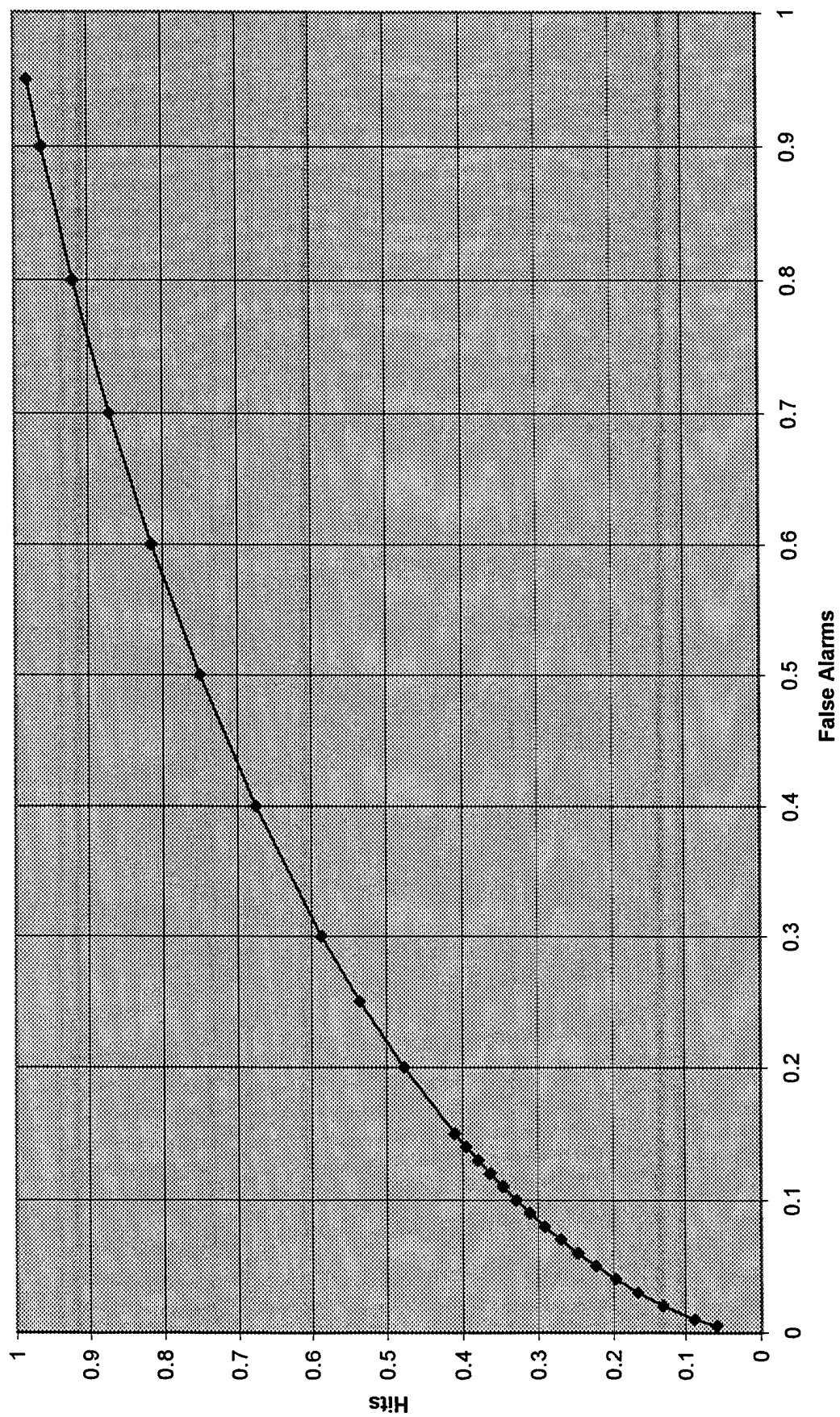


Display D

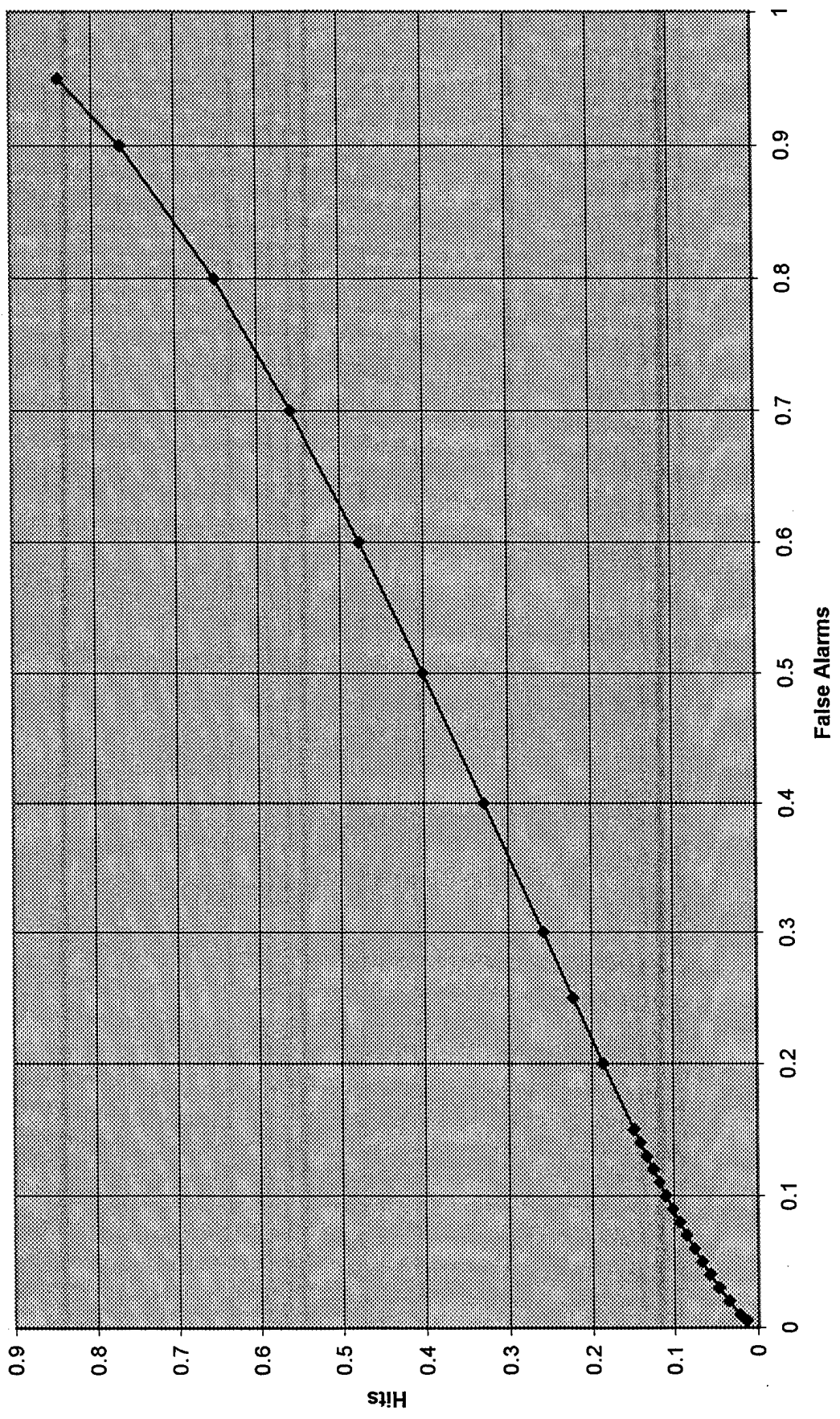
Reader 02 Analog ROC: Type=Diag Area=.8346 STD Area=.0234



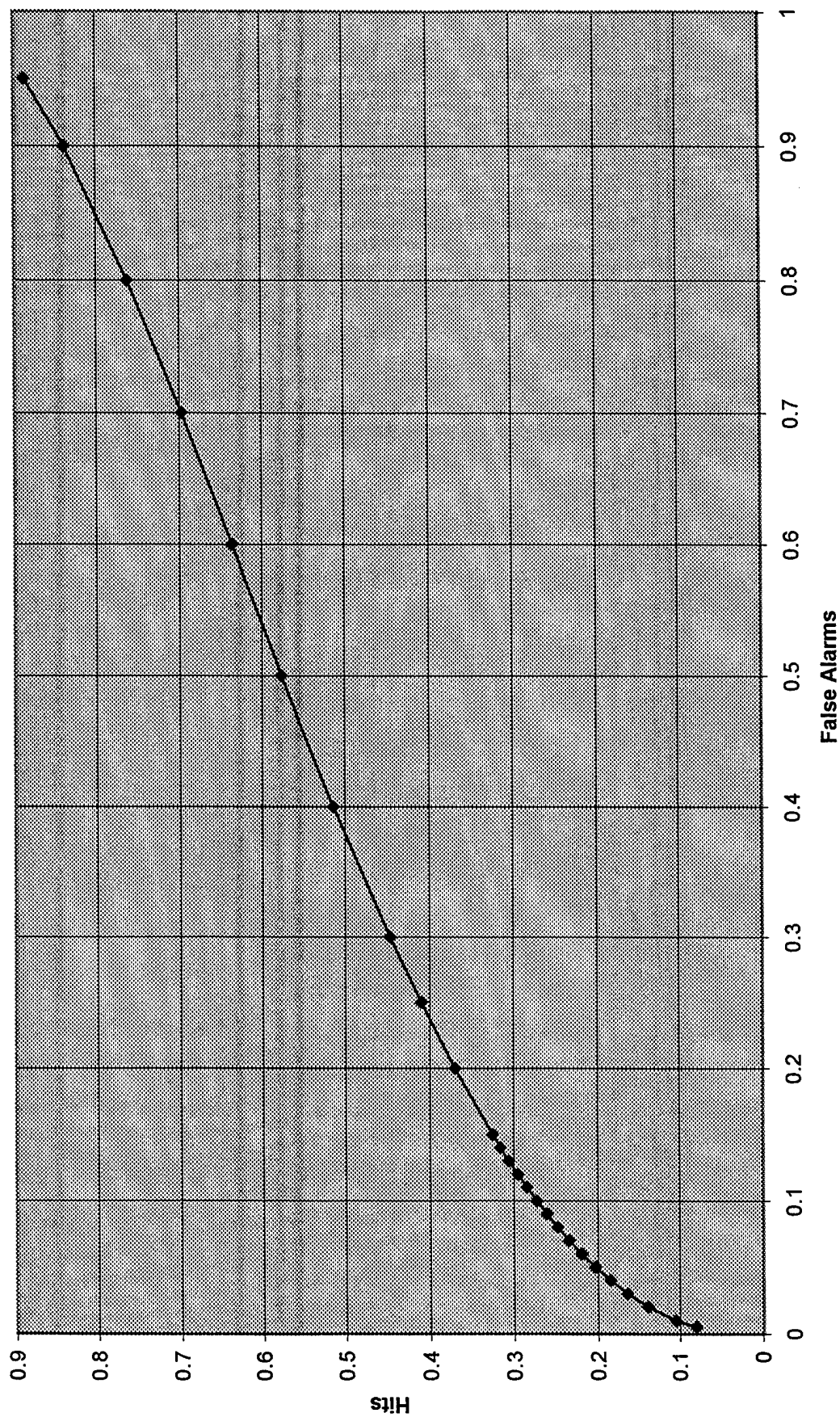
Reader02 Digital ROC: Type=Diag Area=.6949 STD Area=.0398



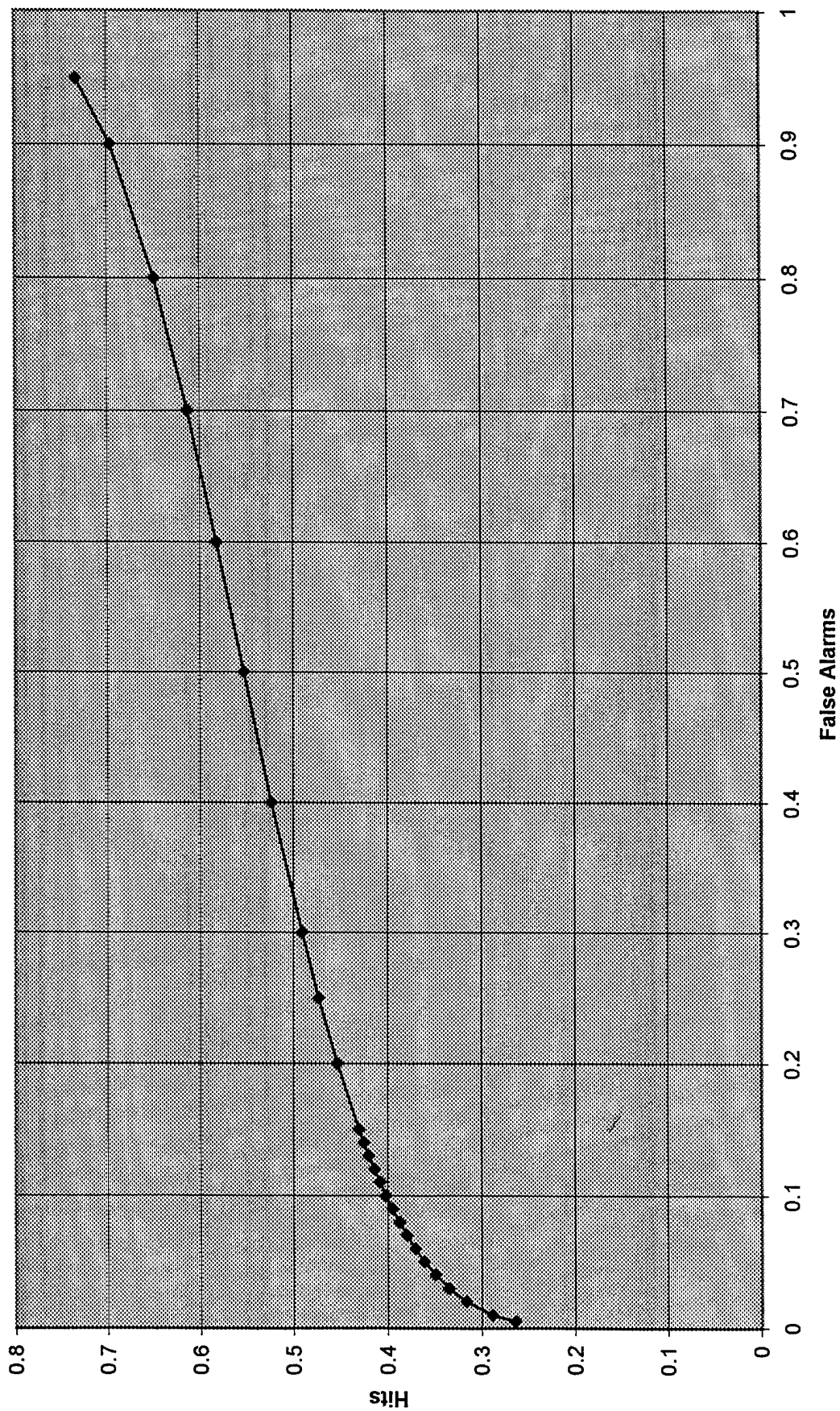
Reader02 Digital ROC: Type=FAD Area=.4210 STD Area=.0487



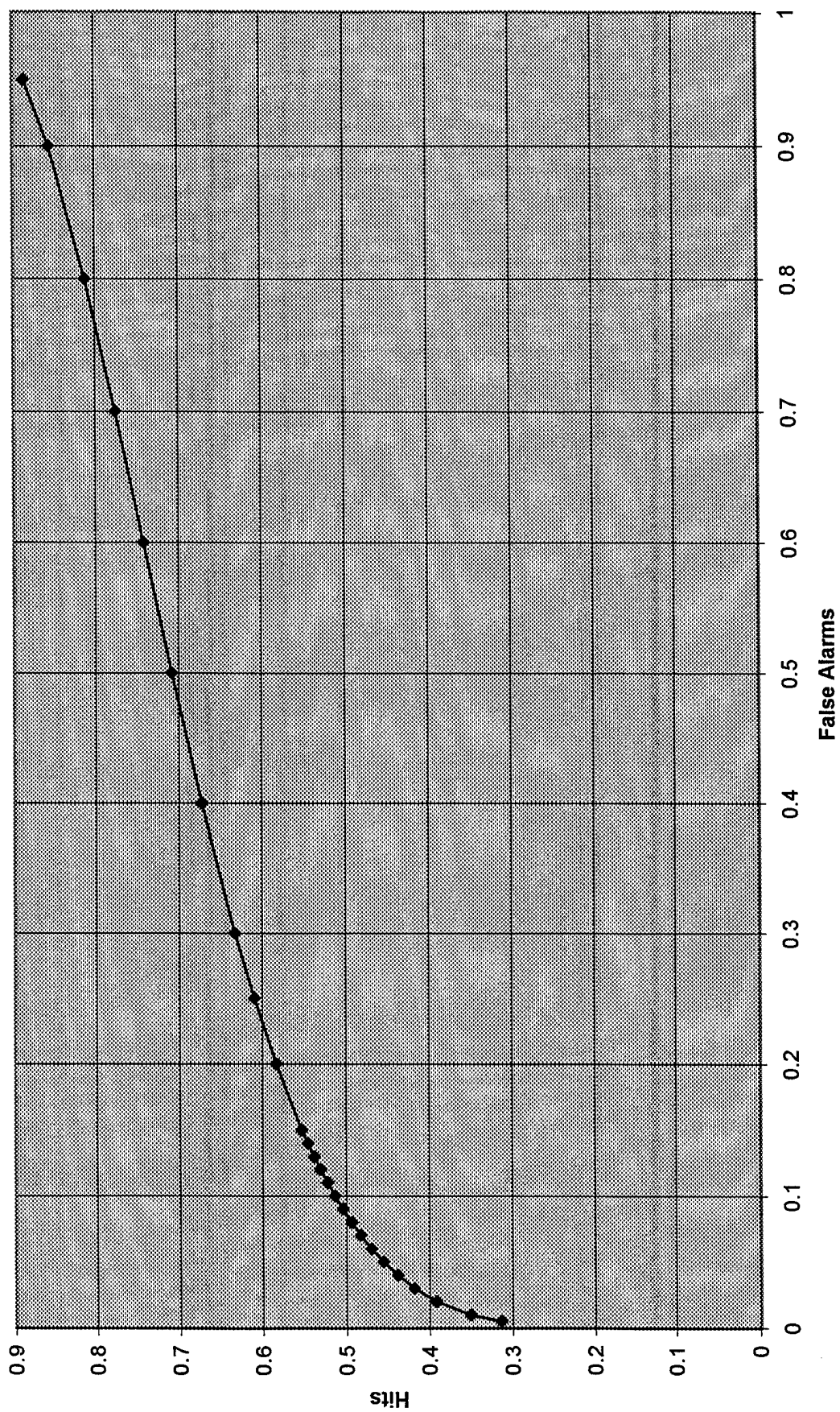
Reader 02 Analog ROC: Type=FAD N=400 Area=.5649 STD Area=.0362



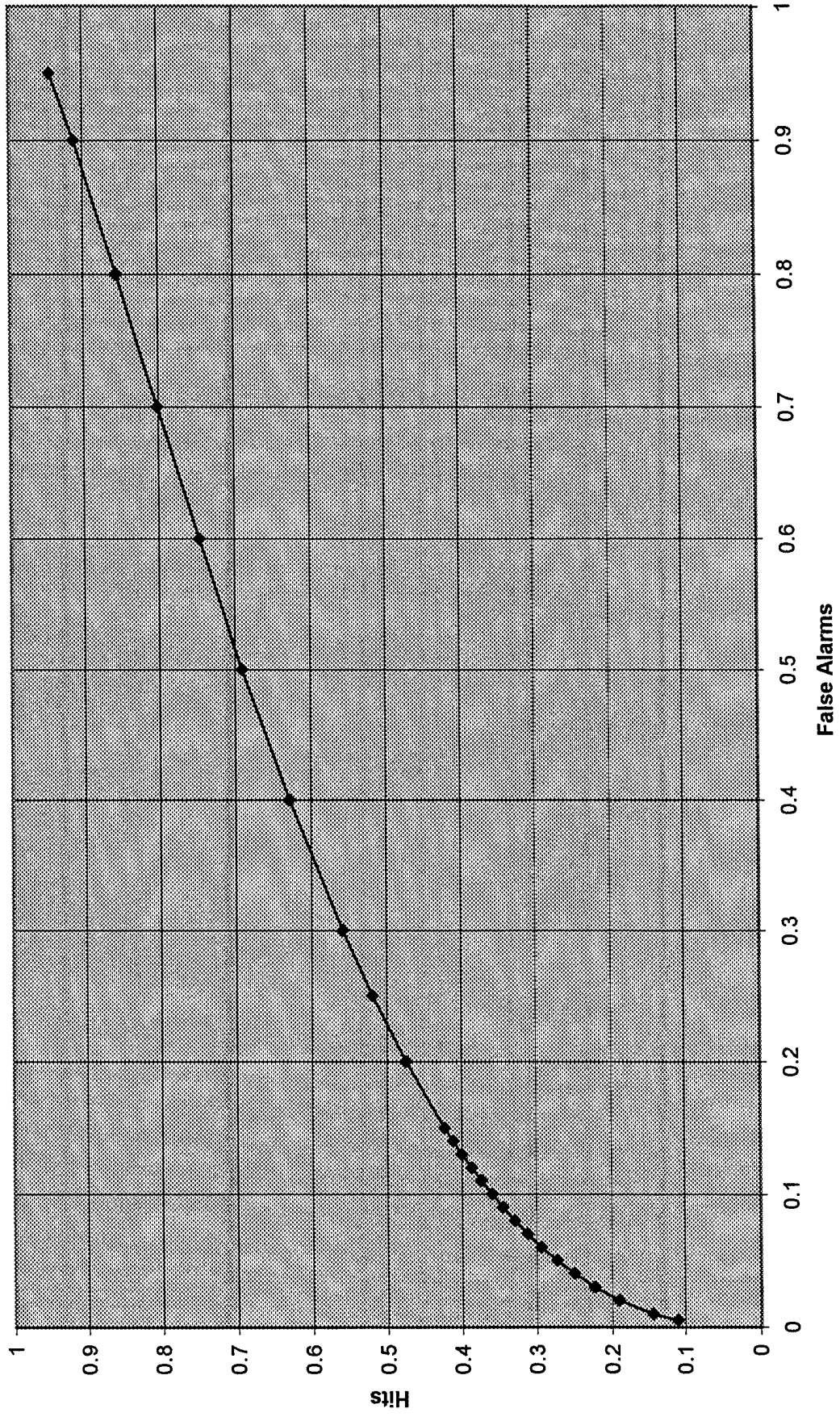
Reader02 Digital ROC: Type=Calc N=200 Area=.5505 STD Area=.0647



Reader02 Analgo ROC: Type=Calc N=400 Area=.6947 STD Area=.0452



Reader 02 Digital ROC: Type= Mass N=200 Area=.6606 STD Area=.0417



Reader 02 Analog ROC: Type=Mass N=400 Area=.6871 STD Area=.0274

